

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

That which is claimed is:

1. (Currently amended) A modified GPCR comprising a ~~NPXXY motif, and a carboxyl terminal tail, wherein said carboxyl terminal tail comprises a putative site of palmitoylation and one or more clusters of phosphorylation,~~

~~wherein the carboxyl terminal tail comprises a retained portion of a carboxyl terminus region of a first GPCR portion fused to a portion of a carboxyl terminus from a second GPCR, and~~

~~wherein the second GPCR comprises the one or more clusters of phosphorylation and further comprises a second putative site of palmitoylation approximately 10 to 25 amino acid residues downstream of a second NPXXY motif.~~
amino acids from a first GPCR and amino acids from a second GPCR, wherein the amino acids from the second GPCR are fused to the amino acids of the first GPCR to yield a modified GPCR,

wherein the amino acids from the first GPCR comprise an NPXXY motif (SEQ. ID NO.: 82)

wherein the amino acids from the second GPCR comprise one or more clusters of phosphorylation, and

wherein the modified GPCR further comprises a putative site of palmitoylation, wherein the putative site of palmitoylation is 10 to 25 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

2. (Previously presented) The modified GPCR of Claim 1, wherein the first GPCR is a Class A receptor.

3. (Previously presented) The modified GPCR of Claim 1, wherein the first GPCR is an olfactory receptor or a taste receptor.

4. (Previously presented) The modified GPCR of Claim 2, wherein the second GPCR is a Class B receptor.

5. (Previously presented) The modified GPCR of Claim 4, wherein the Class B receptor is selected from the group consisting of a vasopressin V2 receptor, a neurotensin-1 receptor, a substance P receptor and an oxytocin receptor.

6. (Previously presented) The modified GPCR of Claim 5, wherein the Class B receptor is a vasopressin V2 receptor.

7. (Currently amended) The modified GPCR of Claim 1, wherein the putative site of palmitoylation is approximately 10 to 25 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

8. (Currently amended) The modified GPCR of Claim 1, wherein the one or more clusters of phosphorylation sites are approximately 20 to 55 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

9. (Currently amended) The modified GPCR of Claim 8, wherein the one or more clusters of phosphorylation sites are approximately 30 to 45 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

10. (Currently amended) The modified GPCR of Claim 1, wherein the one or more clusters of phosphorylation sites are approximately 15 to 35 amino acid residues downstream of the putative site of palmitoylation.

11. (Currently amended) The modified GPCR of Claim 10, wherein the one or more clusters of phosphorylation sites are approximately 15 to 25 amino acid residues downstream of the putative site of palmitoylation.

12. (Currently amended) The modified GPCR of Claim 2, wherein the Class A receptor portion comprises amino acid residues from the NPXXY motif (SEQ. ID NO.: 82) through a cysteine residue approximately 15 to 20 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

13. (Previously presented) The modified GPCR of Claim 4, wherein the Class B receptor portion comprises amino acid residues beginning with an amino acid residue immediately downstream of the second putative site of palmitoylation through a carboxyl-terminal end.

14. (Previously presented) The modified GPCR of Claim 1, wherein the carboxyl terminal tail comprises one or more additions, substitutions or deletions of amino acid residues.

15. (Previously presented) The modified GPCR of Claim 1 comprising a polypeptide with the amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6.

16. (Currently amended) ~~The modified GPCR of Claim 1 conjugated to a detectable molecule.~~ A modified GPCR comprising amino acids from a first GPCR and amino acids from a second GPCR, wherein amino acids from the second GPCR are fused to the first GPCR to yield a modified GPCR,

wherein the amino acids from the first GPCR comprise an NPXXY motif (SEQ. ID NO.: 82),

wherein the amino acids from the second GPCR comprise one or more clusters of phosphorylation,

wherein the modified GPCR further comprises a putative site of palmitoylation, wherein the putative site of palmitoylation is 10 to 25 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82), and

wherein the modified GPCR is conjugated to a detectable molecule.

17. (Currently amended) ~~An isolated nucleic acid sequence encoding the a modified GPCR of Claim 1.~~ wherein the modified GPCR comprises amino acids from a first GPCR and amino acids from a second GPCR, wherein amino acids from the second GPCR are fused to the first GPCR to yield a modified GPCR,

wherein the amino acids from the first GPCR comprise an NPXXY motif (SEQ. ID NO.: 82),

wherein the amino acids from the second GPCR comprise one or more clusters of phosphorylation, and

wherein the modified GPCR further comprises a putative site of palmitoylation, wherein the putative site of palmitoylation is 10 to 25 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

18. (Currently amended) ~~An expression vector comprising the an isolated nucleic acid of Claim 17 operably linked to an expression control sequence.~~ encoding

a modified GPCR, wherein the modified GPCR comprises amino acids from a first GPCR and amino acids from a second GPCR, wherein amino acids from the second GPCR are fused to the first GPCR to yield a modified GPCR,

wherein the amino acids from the first GPCR comprise an NPXXY motif (SEQ. ID NO.: 82),

wherein the amino acids from the second GPCR comprise one or more clusters of phosphorylation,

wherein the modified GPCR further comprises a putative site of palmitoylation, wherein the putative site of palmitoylation is 10 to 25 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82), and

wherein the nucleic acid is operably linked to an expression control sequence.

19. (Currently amended) A host cell comprising the an expression vector of Claim 18, comprising an isolated nucleic acid encoding a modified GPCR, wherein the modified GPCR comprises amino acids from a first GPCR and amino acids from a second GPCR, wherein amino acids from the second GPCR are fused to the first GPCR to yield a modified GPCR,

wherein the amino acids from the first GPCR comprise an NPXXY motif (SEQ. ID NO.: 82),

wherein the amino acids from the second GPCR comprise one or more clusters of phosphorylation,

wherein the modified GPCR further comprises a putative site of palmitoylation, wherein the putative site of palmitoylation is 10 to 25 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82), and

wherein the nucleic acid is operably linked to an expression control sequence.

20. (Currently amended) A modified GPCR comprising a NPXXY motif (SEQ. ID NO.: 82) and a carboxyl terminal tail,

wherein the carboxyl terminal tail comprises a putative site of palmitoylation and one or more clusters of phosphorylation,

wherein the carboxyl terminal tail comprises a retained portion of a carboxyl-terminus region of a first GPCR portion fused to a polypeptide,

wherein the polypeptide comprises the one or more clusters of phosphorylation, and

wherein the retained portion of the first GPCR and the polypeptide are fused at an amino acid residue adjacent to the putative site of palmitoylation.

21. (Currently amended) The modified GPCR of claim 20, wherein the one or more clusters of phosphorylation sites are from a second GPCR portion and wherein the second GPCR further comprises a second putative site of palmitoylation approximately 10 to 25 amino acid residues downstream of a second NPXXY motif (SEQ. ID NO.: 82).

22. (Previously presented) The modified GPCR of claim 20, wherein the first GPCR is a Class A receptor.

23. (Previously presented) The modified GPCR of claim 21, wherein the second GPCR is a Class B receptor.

24. (Currently amended) The modified GPCR of Claim 20, wherein the one or more clusters of phosphorylation sites are 20 to 55 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

25. (Previously presented) The modified GPCR of Claim 20, wherein the one or more clusters of phosphorylation sites are 15 to 35 amino acid residues downstream of the putative site of palmitoylation.

26. (Currently amended) A modified GPCR comprising a NPXXY motif (SEQ. ID NO.: 82) and a carboxyl terminal tail,

wherein said carboxyl terminal tail comprises a palmitoylated cysteine residue and one or more clusters of phosphorylation,

wherein the carboxyl terminal tail comprises a retained portion of a carboxyl-terminus region of a first GPCR portion fused to a portion of a carboxyl-terminus from a second GPCR, and

wherein said second GPCR comprises the one or more clusters of phosphorylation, and

wherein the retained portion of said first GPCR and said second GPCR are fused at an amino acid residue adjacent to the palmitoylated cysteine residue.

27. (Previously presented) The modified GPCR of claim 26, wherein the first GPCR is a Class A receptor and the second GPCR is a Class B receptor.

28. (Previously presented) The modified GPCR of claim 27, wherein the retained portion ends with the palmitoylated cysteine residue and the second GPCR begins with an amino acid residue immediately downstream of the palmitoylated cysteine residue.

29. (Currently amended) The modified GPCR of Claim 27, wherein the one or more clusters of phosphorylation sites are 20 to 55 amino acid residues downstream of the NPXXY motif (SEQ. ID NO.: 82).

30. (Withdrawn) The modified GPCR of Claim 27, wherein the one or more clusters of phosphorylation sites are 15 to 35 amino acid residues downstream of the putative site of palmitoylation.

31. (Withdrawn) A method of screening compounds for GPCR activity comprising the steps of:

- (a) providing a cell that expresses at least one modified GPCR according to claim 1, wherein said cell further comprises arrestin conjugated to a detectable molecule;
- (b) exposing the cell to the compound;
- (c) detecting location of the arrestin within the cell;
- (d) comparing the location of the arrestin within the cell in the presence of the compound to the location of the arrestin within the cell in the absence of the compound; and
- (e) correlating a difference between (1) the location of the arrestin within the cell in the presence of the compound and (2) the presence of the location of the arrestin within the cell in the absence of the compound.

32. (Withdrawn) The method of Claim 31, wherein the arrestin is detected in endosomes.

33. (Withdrawn) A compound identified by the method of Claim 31.

34. (Withdrawn) A pharmaceutical composition for the treatment of a disease associated with GPCR activity in mammals, comprising a therapeutically effective amount of a compound according to Claim 33 and a pharmaceutically acceptable carrier.

35. (Withdrawn) A method of preventing and/or treating a disease associated with GPCR in mammals, comprising administering to a mammal an amount of the pharmaceutical composition of Claim 34 sufficient to reduce or alleviate symptoms of said disease.

36. (Withdrawn) A method of preventing and/or treating a disease associated with GPCR in mammals, comprising administering to a mammal an amount of the isolated nucleic acid of Claim 17 sufficient to reduce or alleviate symptoms of said disease.

37. (Withdrawn) A kit for identifying a molecule that modulates the activity of a GPCR, comprising a cell that expresses at least one modified GPCR according to Claim 1, wherein said cell further comprises arrestin conjugated to a detectable molecule.

38. (New) The modified GPCR of claim 1, wherein the putative site of palmitoylation is from the first GPCR.

39. (New) The modified GPCR of claim 1, wherein the putative site of palmitoylation is from the second GPCR.